

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

- 1-47. (Withdrawn)
- 48. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, the ~~beta-secretase encoding~~ sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 43 or a perfect complementary sequence of any of such nucleotides.
- 49-50. (Canceled)
- 51. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 48 and a promoter, wherein the nucleic acid and the promoter are operably linked.
- 52. (Original) The recombinant expression vector of claim 51, wherein said vector is suitable for transfection of a bacterial cell.
- 53. (Original) A heterologous cell transfected with the vector of claim 51, wherein said cell expresses a biologically active  $\beta$ -secretase.
- 54. (Original) The cell of claim 53, wherein said cell is a eukaryotic cell.
- 55. (Original) The cell of claim 53, wherein said cell is a bacterial cell.
- 56. (Original) The cell of claim 53, wherein said cell is an insect cell.
- 57. (Original) The cell of claim 53, wherein said cell is a yeast cell.
- 58. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase that consists of nucleotides encoding ~~that encodes~~ SEQ ID NO: 43 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.
- 59. (Original) The method of claim 58, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

60. (Previously presented) The method of claim 59, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

61. (Original) The method of claim 58, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

62. (Previously presented) The method of claim 61, wherein said antibody binds specifically to SEQ ID NO: 43.

63. (Previously presented) The method of claim 61, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

64. (Currently amended) A heterologous cell, comprising  
(i) a nucleic acid molecule comprising nucleotides encoding beta secretase consisting of nucleotides encoding SEQ ID NO: 43 or the complementary sequence of said nucleic acid molecule;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

65. (Original) The cell of claim 64, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

66. (Previously presented) The cell of claim 64, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

67. (Original) The cell of claim 64, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

68. (Previously presented) The cell of claim 64, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

69. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 82.

70-113. (Canceled)

114. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, ~~the beta-secretase encoding the~~ sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 58 or a perfect complementary sequence of any of such nucleotides.

115. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 114 and a promoter, wherein the nucleic acid and the promoter are operably linked.

116. (Previously presented) The expression vector of claim 115, wherein said vector is suitable for transfection of a bacterial cell.

117. (Previously presented) A heterologous cell transfected with the vector of claim 115, wherein said cell expresses a biologically active  $\beta$ -secretase.

118. (Previously presented) The cell of claim 117, wherein said cell is a eukaryotic cell.

119. (Previously presented) The cell of claim 117, wherein said cell is a bacterial cell.

120. (Previously presented) The cell of claim 117, wherein said cell is an insect cell.

121. (Previously presented) The cell of claim 117, wherein said cell is a yeast cell.

122. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, ~~the beta-secretase encoding the~~ sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 59 or a perfect complementary sequence of any of such nucleotides.

123. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 122 and a promoter, wherein the nucleic acid and the promoter are operably linked.

124. (Previously presented) The expression vector of claim 123, wherein said vector is suitable for transfection of a bacterial cell.

125. (Previously presented) A heterologous cell transfected with the vector of claim 123, wherein said cell expresses a biologically active  $\beta$ -secretase.

126. (Previously presented) The cell of claim 125, wherein said cell is a eukaryotic cell.

127. (Previously presented) The cell of claim claim 125, wherein said cell is a bacterial cell.

128. (Previously presented) The cell of claim 125, wherein said cell is an insect cell.

129. (Previously presented) The cell of claim 125, wherein said cell is a yeast cell.

130. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, ~~the beta-secretase encoding the~~ sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 66 or a perfect complementary sequence of any of such nucleotides.

131. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 130 and a promoter, wherein the nucleic acid and the promoter are operably linked.

132. (Previously presented) The expression vector of claim 131, wherein said vector is suitable for transfection of a bacterial cell.

133. (Previously presented) A heterologous cell transfected with the vector of claim 130, wherein said cell expresses a biologically active  $\beta$ -secretase.

134. (Previously presented) The cell of claim 133, wherein said cell is a eukaryotic cell.

135. (Previously presented) The cell of claim 133, wherein said cell is a bacterial cell.

136. (Previously presented) The cell of claim 133, wherein said cell is an insect cell.

137. (Previously presented) The cell of claim 133, wherein said cell is a yeast cell.

138. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, the ~~beta-secretase encoding~~ sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 67 or a perfect complementary sequence of any of such nucleotides.

139. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 138 and a promoter, wherein the nucleic acid and the promoter are operably linked.

140. (Previously presented) The expression vector of claim 139, wherein said vector is suitable for transfection of a bacterial cell.

141. (Previously presented) A heterologous cell transfected with the vector of claim 139, wherein said cell expresses a biologically active  $\beta$ -secretase.

142. (Previously presented) The cell of claim 141, wherein said cell is a eukaryotic cell.

143. (Previously presented) The cell of claim 141, wherein said cell is a bacterial cell.

144. (Previously presented) The cell of claim 141, wherein said cell is an insect cell.

145. (Previously presented) The cell of claim 141, wherein said cell is a yeast cell.

146. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, the ~~beta-secretase encoding~~

sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 68 or a perfect complementary sequence of any of such nucleotides.

147. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 146, and a promoter, wherein the nucleic acid and the promoter are operably linked.

148. (Previously presented) The expression vector of claim 147, wherein said vector is suitable for transfection of a bacterial cell.

150. (Previously presented) A heterologous cell transfected with the vector of claim 147, wherein said cell expresses a biologically active  $\beta$ -secretase.

150. (Previously presented) The cell of claim 149, wherein said cell is a eukaryotic cell.

151. (Previously presented) The cell of claim 149, wherein said cell is a bacterial cell.

152. (Previously presented) The cell of claim 149, wherein said cell is an insect cell.

153. (Previously presented) The cell of claim 149, wherein said cell is a yeast cell.

154. (Currently amended) An isolated nucleic acid, comprising a sequence of ~~beta-secretase encoding~~ nucleotides encoding beta secretase, the sequence of ~~beta-secretase encoding~~ nucleotides consisting of nucleotides encoding SEQ ID NO: 69 or a perfect complementary sequence of any of such nucleotides.

155. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 154, and a promoter, wherein the nucleic acid and the promoter are operably linked.

156. (Previously presented) The expression vector of claim 155, wherein said vector is suitable for transfection of a bacterial cell.

157. (Previously presented) A heterologous cell transfected with the vector of claim 155, wherein said cell expresses a biologically active  $\beta$ -secretase.

158. (Previously presented) The cell of claim 157, wherein said cell is a eukaryotic cell.
159. (Previously presented) The cell of claim 157, wherein said cell is a bacterial cell.
160. (Previously presented) The cell of claim 157, wherein said cell is an insect cell.
161. (Previously presented) The cell of claim 157, wherein said cell is a yeast cell.
162. (Currently amended) An isolated nucleic acid, comprising a sequence ~~beta-secretase encoding~~ of nucleotides encoding beta secretase, the sequence ~~beta-secretase encoding~~ nucleotides consisting of nucleotides encoding SEQ ID NO: 70 or a perfect complementary sequence of any of such nucleotides.
163. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 162, and a promoter, wherein the nucleic acid and the promoter are operably linked.
164. (Previously presented) The expression vector of claim 162, wherein said vector is suitable for transfection of a bacterial cell.
165. (Previously presented) A heterologous cell transfected with the vector of claim 163, wherein said cell expresses a biologically active  $\beta$ -secretase.
166. (Previously presented) The cell of claim 165, wherein said cell is a eukaryotic cell.
167. (Previously presented) The cell of claim 165, wherein said cell is a bacterial cell.
168. (Previously presented) The cell of claim 165, wherein said cell is an insect cell.
169. (Previously presented) The cell of claim 165, wherein said cell is a yeast cell.

170. (Currently amended) An isolated nucleic acid, comprising a sequence ~~beta-secretase encoding of~~ nucleotides encoding beta secretase, ~~the beta-secretase encoding sequence of~~ nucleotides consisting of nucleotides encoding SEQ ID NO: 74 or a perfect complementary sequence of any of such nucleotides

171. (Previously presented) An expression vector, comprising the isolated nucleic acid of claim 170, and a promoter, wherein the nucleic acid and the promoter are operably linked.

172. (Previously presented) The expression vector of claim 171, wherein said vector is suitable for transfection of a bacterial cell.

173. (Previously presented) A heterologous cell transfected with the vector of claim 171, wherein said cell expresses a biologically active  $\beta$ -secretase.

174. (Previously presented) The cell of claim 173, wherein said cell is a eukaryotic cell.

175. (Previously presented) The cell of claim 173, wherein said cell is a bacterial cell.

176. (Previously presented) The cell of claim 173, wherein said cell is an insect cell.

177. (Previously presented) The cell of claim 173, wherein said cell is a yeast cell.

178. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secrease, the sequence of nucleotides consisting of nucleotides encoding that encodes SEQ ID NO: 58 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

179. (Previously presented) The method of claim 178, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.



180. (Previously presented) The method of claim 179, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

181. (Previously presented) The method of claim 178, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

182. (Previously presented) The method of claim 181, wherein said antibody binds specifically to SEQ ID NO: 58.

183. (Previously presented) The method of claim 181, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

184. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase the sequence of nucleotides consisting of nucleotides encoding ~~that encodes~~ SEQ ID NO: 59 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

185. (Previously presented) The method of claim 184, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

186. (Previously presented) The method of claim 185, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

187. (Previously presented) The method of claim 184, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

188. (Previously presented) The method of claim 187, wherein said antibody binds specifically to SEQ ID NO: 59.

189. (Previously presented) The method of claim 187, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

190. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase, the sequence of nucleotides consisting of nucleotides that encodes- encoding SEQ ID NO: 66 or a complementary sequence of such nucleotides under

conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

191. (Previously presented) The method of claim 190, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

192. (Previously presented) The method of claim 191,, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

193. (Previously presented) The method of claim 190, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

194. (Previously presented) The method of claim 193, wherein said antibody binds specifically to SEQ ID NO: 66.

195. (Previously presented) The method of claim 193, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

196. (Previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase, the sequence of nucleotide consisting of nucleotides encoding that encodes SEQ ID NO: 67 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

197. (Previously presented) The method of claim 196, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

198. (Previously presented) The method of claim 197, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

199. (Previously presented) The method of claim 196, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

200. (Previously presented) The method of claim 199, wherein said antibody binds specifically to SEQ ID NO: 67.

201. (Previously presented) The method of claim 196, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

202. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase the sequence of nucleotides consisting of nucleotides that encodes encoding SEQ ID NO: 68 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

203. (Previously presented) The method of claim 202, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

204. (Previously presented) The method of claim 203, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

205. (Previously presented) The method of claim 202, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

206. (Previously presented) The method of claim 205,, wherein said antibody binds specifically to SEQ ID NO: 68.

207. (Previously presented) The method of claim 205, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

208. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase, the sequence of nucleotides consisting of nucleotides that encodes encoding SEQ ID NO: 69 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

209. (Previously presented) The method of claim 208, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

210. (Previously presented) The method of claim 209, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

211. (Previously presented) The method of claim 210, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

212. (Previously presented) The method of claim 208, wherein said antibody binds specifically to SEQ ID NO: 69.

213. (Previously presented) The method of claim 211, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

214. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase, the sequence of nucleotides consisting of nucleotides that encodes encoding SEQ ID NO: 70 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

215. (Previously presented) The method of claim 214, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

216. (Previously presented) The method of claim 215, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

217. (Previously presented) The method of claim 214, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

218. (Previously presented) The method of claim 217, wherein said antibody binds specifically to SEQ ID NO: 70.

219. (Previously presented) The method of claim 217, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

220. (Currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides encoding beta secretase, the sequence of nucleotides consisting of nucleotides that encodes encoding SEQ ID NO: 74 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

221. (Previously presented) The method of claim 220, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

222. (Previously presented) The method of claim 221, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

223. (Previously presented) The method of claim 220, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

224. (Previously presented) The method of claim 223, wherein said antibody binds specifically to SEQ ID NO: 74.

225. (Previously presented) The method of claim 220, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

226. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

227. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

228. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

229. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

230. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

231. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

232. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

233. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

234. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

235. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

236. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

237. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

238. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

239. (Previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

240. (Currently amended) A heterologous cell, comprising  
(i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 58 or the complementary sequence of said nucleic acid molecule;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

241. (Previously presented) The cell of claim 240, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

242. (Previously presented) The cell of claim 240, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

243. (Previously presented) The cell of claim 240, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

244. (Previously presented) The cell of claim 240, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

245. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

246. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

247. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

248. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

249. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

250. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

251. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

252. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

253. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

254. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

255. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

256. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

257. (Previously presented) The cell claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

258. (Previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

259. (Currently amended) A heterologous cell, comprising
- (i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 59 or the complementary sequence of said nucleic acid molecule;
  - (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
  - (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.
260. (Previously presented) The cell of claim 259, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.
261. (Previously presented) The cell of claim 259, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.
262. (Previously presented) The cell of claim 259, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.
263. (Previously presented) The cell of claim 259, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).
264. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.
265. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.
268. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.
267. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.



268. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

269. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

270. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

271. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

272. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

273. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

274. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

275. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

276. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

277. (Previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

278. (Currently amended) A heterologous cell, comprising

- (i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 66 or the complementary sequence of said nucleic acid molecule;
- (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

279. (Previously presented) The cell of claim 278, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

280. (Previously presented) The cell of claim 278, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

281. (Previously presented) The cell of claim 278, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

282. (Previously presented) The cell of claim 278, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

283. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

284. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

285. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

286. (Previously presented) The cell of claim 281,, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

287. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

288. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

289. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

290. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

291. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

292. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

293. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

294. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

295. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

296. (Previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

297. (Currently amended) A heterologous cell, comprising  
(i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 67 or the complementary sequence of said nucleic acid molecule;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

298. (Previously presented) The cell of claim 297, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

299. (Previously presented) The cell of claim 297, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

300. (Previously presented) The cell of claim 297, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

301. (Previously presented) The cell of claim 297, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

302. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

303. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

304.. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

305. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

306. (Previously presented) The cell of claim 300,, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

307. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

308. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

309. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

310. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

311. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

312. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

311. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

312. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

313. (Previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

314. (Currently amended) A heterologous cell, comprising  
(i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 68 or the complementary sequence of said nucleic acid molecule;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

315. (Previously presented) The cell of claim 314, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

316. (Previously presented) The cell of claim 314, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

317. (Previously presented) The cell of claim 314, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

318. (Previously presented) The cell of claim 314, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

319. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

320. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

321. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

322. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

323. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

324. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

325. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

326. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

327. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

328. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

329. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

330. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

331. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

332. (Previously presented) The cell of claim 317, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

333. (Currently amended) A heterologous cell, comprising
- (i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 69 or the complementary sequence of said nucleic acid molecule;
  - (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
  - (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.
334. (Previously presented) The cell of claim 333, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.
335. (Previously presented) The cell of claim 333, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.
336. (Previously presented) The cell of claim 333, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.
337. (Previously presented) The cell of claim 333, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).
338. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.
339. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.
340. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.
341. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

342. (Previously presented) The cell of claim 336,, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

343. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

344. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

345. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

346. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

347. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

348. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

349. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

350. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

351. (Previously presented) The cell of claim 336, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

352. (Currently amended) A heterologous cell, comprising

(i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 70 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.



353. (Previously presented) The cell of claim 352, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

354. (Previously presented) The cell of claim 352, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

355. (Previously presented) The cell of claim 352, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

356. (Previously presented) The cell of claim 352, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

357. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

358. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

359. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

360. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

361. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

362. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

363. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

364. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

365. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

366. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

367. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

368. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

369. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

370. (Previously presented) The cell of claim 355, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

371. (Currently amended) A heterologous cell, comprising

(i) a nucleic acid molecule encoding beta secretase, the sequence of nucleotides consisting of nucleotides encoding SEQ ID NO: 74 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

372. (Previously presented) The cell of claim 371, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

373. (Previously presented) The cell of claim 371, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

374. (Previously presented) The cell of claim 371, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

375. (Previously presented) The cell of claim 371, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

376. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

377. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

378. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

379. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

380. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

381. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

382. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

383. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

384. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

385. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

386. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

387. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

388. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

389. (Previously presented) The cell of claim 374, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.